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(FILE 'HOME' ENTERED AT 16:09:22 ON 31 MAR 2003)

FILE 'EUROPATFULL, PCTFULL, USPATFULL, USPAT2, WPIDS' ENTERED AT 16:09:51

ON 31 MAR 2003

E GRAHAM B/IN

L1 57 S E3-E12  
L2 0 S L1 AND (VIRUS OR VIRAL)

FILE 'MEDLINE, EMBASE, BIOSIS' ENTERED AT 16:11:03 ON 31 MAR 2003

E GRAHAM B/AU

L3 465 S E3-E12  
L4 73 S L3 AND (VIRUS OR VIRAL)  
L5 0 S L4 AND HMG?  
L6 0 S L4 AND (?STATIN)  
L7 1498 S (?STATIN) (L) (VIRUS OR VIRAL)  
L8 35 S L7 (L) HMG?  
L9 12 S L8 NOT PY>=2000

FILE 'EUROPATFULL, PCTFULL, USPATFULL, USPAT2, WPIDS' ENTERED AT 16:18:24

ON 31 MAR 2003

L10 369 S L9  
L11 2145 S (?STATIN) (S) (VIRUS OR VIRAL)  
L12 0 S L11 (S) ( (HMG(2W) COA) (4A) INHITIT?)  
L13 42 S L11 (S) (HMG(2W) COA)  
L14 10 S L13 NOT PY>=2000  
L15 5131 S LOVASTATIN OR SIMVASTATIN OR FLUVASTATIN OR ATORVASTATIN OR P  
L16 146 S L15 (S) (VIRUS OR VIRAL)  
L17 33 S L16 NOT PY>=2000  
L18 15 S L16/CLM  
L19 5 S L18 NOT PY>=2000

FILE 'MEDLINE, EMBASE, BIOSIS' ENTERED AT 16:38:53 ON 31 MAR 2003

L20 935081 S 17  
L21 47 S L17  
L22 0 S L21 AND (RSV OR RESPIRATORY(W) SYNCYTIAL)  
L23 7 S L16 AND (RSV OR RESPIRATORY(W) SYNCYTIAL)

FILE 'EUROPATFULL, PCTFULL, USPATFULL, USPAT2, WPIDS' ENTERED AT 16:46:21

ON 31 MAR 2003

=> s 23

L24 2943448 23

=> s l23

L25 8 L23

=> s ibib 1-8

L26 1 IBIB 1-8

=> d l25 ibib 1-8

L25 ANSWER 1 OF 8 PCTFULL COPYRIGHT 2003 Univentio  
ACCESSION NUMBER: 2002069977 PCTFULL ED 20020926 EW 200237  
TITLE (ENGLISH): USE OF CERTAIN STEROIDS FOR TREATMENT OF BLOOD CELL

TITLE (FRENCH): DEFICIENCIES  
 TRAITEMENT DE DEFICIENCES AFFECTANT LES GLOBULES  
 SANGUINS  
 INVENTOR(S): AHLEM, Clarence, N., 8960 Montrose Way, San Diego, CA  
 92122, US;  
 READING, Christopher, P.O. Box 12511, San Diego, CA  
 92122, US;  
 FRINCKE, James, P.O. Box 927420, San Diego, CA 92192,  
 US;  
 STICKNEY, Dwight, 5275 Ashby Lane, Granite Bay, CA  
 95746, US;  
 LARDY, Henry, 1829 Thorstand Road, Madison, WI 53705,  
 US;  
 MARWAH, Padma, 6710 Spring Grove Court, Middleton, WI  
 53562, US;  
 MARWAH, Ashok, 6710 Spring Grove Court, Middleton, WI  
 53562, US;  
 PRENDERGAST, Patrick, T., Baybush, Straffan, County  
 Kildare, IE  
 PATENT ASSIGNEE(S): HOLLIS-EDEN PHARMACEUTICALS, INC., Suite 400, 4435  
 Eastgate Mall, San Diego, CA 92121, US [US, US]  
 AGENT: MUENCHAU, Daryl\$, Hollis-Eden Pharmaceuticals, Inc.,  
 Suite 400, 4435 Eastgate Mall, San Diego, CA 92121\$,  
 US  
 LANGUAGE OF FILING: English  
 LANGUAGE OF PUBL.: English  
 DOCUMENT TYPE: Patent  
 PATENT INFORMATION:

	NUMBER	KIND	DATE
	-----		
	WO 2002069977	A1	20020912
DESIGNATED STATES			
W:	AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG UZ VN YU ZA ZM ZW		
RW (ARIPO):	GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW		
RW (EAPO):	AM AZ BY KG KZ MD RU TJ TM		
RW (EPO):	AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR		
RW (OAPI):	BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG		
APPLICATION INFO.:	WO 2002-US6708	A	20020301
PRIORITY INFO.:	US 2001-60/272,624		20010301
	US 2001-09/820,483		20010329
	US 2001-60/323,016		20010910
	US 2001-60/328,738		20011011
	US 2001-60/340,054		20011101
	US 2001-60/338,015		20011108
	US 2001-60/343,523		20011220

=> s e1-e35

727 1068-55-9/BI  
396 135371-29-8/BI  
1805 13734-41-3/BI  
60 149910-63-4/BI  
2 158861-33-7/BI  

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13 160141-19-5/BI  
13 160141-20-8/BI  
12 160141-21-9/BI  
5 160141-46-8/BI  
5 160141-47-9/BI  
5 160141-48-0/BI  
5 160141-49-1/BI  
3 169168-10-9/BI  
1 169168-11-0/BI  
1 169168-12-1/BI  
2 169168-13-2/BI  
2 169168-14-3/BI  
4 169168-15-4/BI  
4 169168-16-5/BI  
1 169168-17-6/BI  
1 169168-18-7/BI  
1 169168-19-8/BI  
1 169168-20-1/BI  
1 169168-21-2/BI  
1 169168-22-3/BI  
1 169168-23-4/BI  
1 169168-24-5/BI  
1 169168-26-7/BI  
2 169328-13-6/BI  
3438 24424-99-5/BI  
104 24629-25-2/BI  
319 3017-69-4/BI  
775 7517-19-3/BI

e9 →  
e29

DETD . . . can be utilized to  
create expression plasmids for a ras gene include, but are not limited  
to, pCI, pSI, pSport (Promega), pBK-CMV, pBK-RSV (Stratagene),  
pEUK-CI (Clontech), pCMV-LIC (Pharmingen) and  
pcDNA1.1/Amp (Invitrogen).

13

Cell-based in vitro ras prenylation assay

The cell lines used in this assay consist of either Rat1 or  
NIH3T3 cells transformed by either **viral** H-ras; an N-ras  
chimeric gene

in which the C-terminal hypervariable region of v-H-ras was substituted  
with the corresponding region from the N-ras gene; or ras-CVLL  
(SEQ.ID.NO.: 1), a **viral**-H-ras mutant in which the C-terminal  
exon

encodes leucine instead of serine, making the encoded protein a  
substrate

for geranylgeranylation by GGPTase I. . . . ml methionine-free DMEM  
supple-

mented with 10% regular DMEM, 2% fetal bovine serum, 400  
gCi[35S]methionine (1000 Ci/mmol) and test compound(s). Cells  
treated with **lovastatin**, a compound that blocks Ras processing  
in

- 150 -

cells by inhibiting the rate-limiting step in the isoprenoid  
biosynthetic  
pathway (Hancock, J.F. . . .

L25 ANSWER 5 OF 8 PCTFULL COPYRIGHT 2003 Univentio

DETD Table;8  
Gene Oncogene/Virus  
m-Actin H-ras  
Adeno  
v-K-ras  
SV40  
E1A  
myosin Heavy Chain E1A  
Myosin Light Chain v-K-ras  
a-Tropomyosin v-K-ras  
v-H-ras  
V-mos  
v-fms  
v-fes  
v-src  
SV40  
**RSV**  
MyoD1 H-ras  
Myogenin TGFB  
V-fos  
Collagen V-mos  
alDha2 (I) v-frc  
v-ras  
H-2K E1A  
(class 1MHC) Adeno  
Neu E1A  
Phosphoenol pyruvate E1A  
carboxykinase  
Polyoma E1A

Examples of reporter units having regulatory regions that are activated. . .

2) Various temperature sensitive oncogenic proteins and **viruses** have been reported: SV40 T antigen (67); v-abl (68); p53 (69) & Ki-MSV (70). The establishment of tumors using these oncogene forms. . . be effective in reversing the transformed phenotype produced by these oncogenes as well as some human colon tumors (77, 78r 75), Similarly, **Lovastatin** which interferes with the posttranslational modification of the Ras precursor protein inhibits ras activation in mammalian cells (80).

L25 ANSWER 5 OF 8

ACCESSION NUMBER:

TITLE (ENGLISH):

TITLE (FRENCH):

INVENTOR(S):

PATENT ASSIGNEE(S):

LANGUAGE OF PUBL.:

DOCUMENT TYPE:

PATENT INFORMATION:

PCTFULL COPYRIGHT 2003 Univentio

1993023533 PCTFULL ED 20020513

ANTI-NEOPLASTIC IN VIVO DRUG SCREEN

TEST IN VIVO DE MEDICAMENTS ANTI-NEOPLASIQUES

LEIBOWITZ, Paul, J.;

WADSWORTH, Samuel;

WOON, Chee-Wai

TSI CORPORATION

English

Patent

NUMBER	KIND	DATE
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WO 9323533	A1	19931125
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DESIGNATED STATES

W:

AU CA FI JP NO AT BE CH DE DK ES FR GB GR IE IT LU MC

NL PT SE

APPLICATION INFO.:

WO 1993-US4363	A	19930507
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PRIORITY INFO.:

US 1992-7/879,933		19920508
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L25        ANSWER 4 OF 8            PCTFULL        COPYRIGHT 2003 Univentio  
ACCESSION NUMBER:            1999010525 PCTFULL    ED 20020515  
TITLE (ENGLISH):            A METHOD OF TREATING CANCER  
TITLE (FRENCH):            PROCEDE POUR LE TRAITEMENT DU CANCER  
INVENTOR(S):                HEIMBROOK, David, C.;

PATENT ASSIGNEE(S) : DeFEO-JONES, Deborah;  
OLIFF, Allen, I.;  
STIRDIVANT, Steven, M.  
MERCK & CO., INC.;  
HEIMBROOK, David, C.;  
DeFEO-JONES, Deborah;  
OLIFF, Allen, I.;  
STIRDIVANT, Steven, M.

LANGUAGE OF PUBL.: English  
DOCUMENT TYPE: Patent  
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9910525	A1	19990304

DESIGNATED STATES  
W:

AL	AM	AU	AZ	BA	BB	BG	BR	BY	CA	CN	CU	CZ	EE	GE	HR	HU	ID
IL	IS	JP	KG	KR	KZ	LC	LK	LR	LT	LV	MD	MG	MK	MN	MX	NO	NZ
PL	RO	RU	SG	SI	SK	SL	TJ	TM	TR	TT	UA	US	UZ	VN	YU	GH	GM
KE	LS	MW	SD	SZ	UG	ZW	AM	AZ	BY	KG	KZ	MD	RU	TJ	TM	AT	BE
CH	CY	DE	DK	ES	FI	FR	GB	GR	IE	IT	LU	MC	NL	PT	SE	BF	BJ
CF	CG	CI	CM	GA	GN	GW	ML	MR	NE	SN	TD	TG					

APPLICATION INFO.:	WO 1998-US17699	A	19980826
PRIORITY INFO.:	US 1997-60/057,102		19970827
	GB 1997-9724299.4		19971118

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L13 42 S L11 (S) (HMG(2W) COA)  
L14 10 S L13 NOT PY>=2000  
L15 5131 S LOVASTATIN OR SIMVASTATIN OR FLUVASTATIN OR ATORVASTATIN OR  
P  
L16 146 S L15 (S) (VIRUS OR VIRAL)  
L17 33 S L16 NOT PY>=2000



L23 ANSWER 7 OF 7 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 2001:194941 BIOSIS

DOCUMENT NUMBER: PREV200100194941

TITLE: Antiviral activity of **lovastatin** against  
**respiratory syncytial virus** in  
vivo and in vitro.

AUTHOR(S): Gower, Tara L.; Graham, Barney S. (1)

CORPORATE SOURCE: (1) Vanderbilt University School of Medicine, 1161 21st  
Ave. South, A-4103 MCN, Nashville, TN, 37232-2582:  
bgraham@mail.nih.gov USA

SOURCE: Antimicrobial Agents and Chemotherapy, (April, 2001) Vol.  
45, No. 4, pp. 1231-1237. print.  
ISSN: 0066-4804.

DOCUMENT TYPE: Article

LANGUAGE: English

SUMMARY LANGUAGE: English

TI Antiviral activity of **lovastatin** against **respiratory  
syncytial virus** in vivo and in vitro.

AB **Respiratory syncytial virus** (RSV)

is an important human pathogen that can cause severe and life-threatening  
respiratory infections in infants and immunocompromised adults. We have  
recently shown that the RSV F glycoprotein, which mediates  
**viral** fusion, binds to RhoA. One of the steps in RhoA activation  
involves isoprenylation at the carboxy terminus of the protein. . .  
allows RhoA to be attached to phosphatidyl serine on the inner leaflet of  
the plasma membrane. Treatment of mice with **lovastatin**, a drug  
that inhibits prenylation pathways in the cell by directly inhibiting  
hydroxymethylglutaryl coenzyme A reductase, diminishes RSV but  
not vaccinia **virus** replication when administered up to 24 h  
after RSV infection and decreases **virus**-induced weight  
loss and illness in mice. The inhibition of replication is not likely due  
to the inhibition of cholesterol biosynthesis, since gemfibrozil, another  
cholesterol-lowering agent, did not affect **virus** replication and  
serum cholesterol levels were not significantly lowered by  
**lovastatin** within the time frame of the experiment.  
**Lovastatin** also reduces cell-to-cell fusion in cell culture and  
eliminates RSV replication in HEp-2 cells. These data indicate  
that **lovastatin**, more specific isoprenylation inhibitors, or  
other pharmacological approaches for preventing RhoA membrane  
localization

should be considered for evaluation as a preventive antiviral therapy for  
selected groups of patients at high risk for severe RSV disease,  
such as the institutionalized elderly and bone marrow or lung transplant  
recipients.

IT Major Concepts

Infection; Pharmacology

IT Diseases

**respiratory syncytial virus** infection: viral  
disease

IT Chemicals & Biochemicals

F glycoprotein; RhoA; cholesterol; lovastatin: HMG CoA reductase  
inhibitor - drug, antiviral - drug

IT Alternate Indexing

**Respiratory Syncytial Virus** Infections (MeSH)

ORGN . . .

Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia;

Paramyxoviridae: Animal Viruses, Viruses, Microorganisms

ORGN Organism Name

HEp-2 cell line (Hominidae); mouse (Muridae); **respiratory**

**syncytial virus (Paramyxoviridae): pathogen**

ORGN Organism Superterms

Animal Viruses; Animals; Chordates; Humans; Mammals; Microorganisms;  
Nonhuman Mammals; Nonhuman Vertebrates; Primates; Rodents;  
Vertebrates;. . .

ACCESSION NUMBER: 1999005161 PCTFULL ED 20020515  
 TITLE (ENGLISH): HUMAN PEROXISOME PROLIFERATOR ACTIVATED RECEPTOR GAMMA  
 (PPAR&gamma;) GENE REGULATORY SEQUENCES AND USES  
 THEREFOR  
 TITLE (FRENCH): SEQUENCES REGULATRICES DU GENE HUMAIN PPAR&gamma;  
 (RECEPTEUR GAMMA ACTIVE DE LA PROLIFERATION DES  
 PEROXYSOMES) ET LEURS UTILISATIONS  
 INVENTOR(S): BRIGGS, Michael, R.;  
 SALADIN, Regis, S.;  
 AUWERX, Johan;  
 FAJAS, Lluís  
 PATENT ASSIGNEE(S): LIGAND PHARMACEUTICALS INCORPORATED;  
 INSTITUT PASTEUR;  
 BRIGGS, Michael, R.;  
 SALADIN, Regis, S.;  
 AUWERX, Johan;  
 FAJAS, Lluís  
 LANGUAGE OF PUBL.: English  
 DOCUMENT TYPE: Patent  
 PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9905161	A1	19990204

DESIGNATED STATES  
 W:

AL	AM	AT	AU	AZ	BA	BB	BG	BR	BY	CA	CH	CN	CU	CZ	DE	DK	EE
ES	FI	GB	GE	GH	GM	HR	HU	ID	IL	IS	JP	KE	KG	KP	KR	KZ	LC
LK	LR	LS	LT	LU	LV	MD	MG	MK	MN	MW	MX	NO	NZ	PL	PT	RO	RU
SD	SE	SG	SI	SK	SL	TJ	TM	TR	TT	UA	UG	US	UZ	VN	YU	ZW	GH
GM	KE	LS	MW	SD	SZ	UG	ZW	AM	AZ	BY	KG	KZ	MD	RU	TJ	TM	AT
BE	CH	CY	DE	DK	ES	FI	FR	GB	GR	IE	IT	LU	MC	NL	PT	SE	BF
BJ	CF	CG	CI	CM	GA	GN	GW	ML	MR	NE	SN	TD	TG				

APPLICATION INFO.: WO 1998-US15411 A 19980724  
 PRIORITY INFO.: US 1997-60/053,692 19970725

4

4, 5, 6, 8.

cholesterol synthesis, provide another way to modify cellular cholesterol levels. Upon treatment, with compounds such as compactin or **simvastatin**, cells will become cholesterol depleted and the production of the active forms of ADD-1/SREBP-1 will increase (Sakai et al., Cell 85:1037-1046. . . . Therefore, the expression of PPAR $\gamma$  protein was evaluated in Hep G2 cells before and after treatment with the potent HMG-CoA reductase inhibitor, **simvastatin**. Treatment of the cells with **simvastatin** (5 x 10<sup>-6</sup> M) during 6 hours resulted in a robust and fast induction of PPAR $\gamma$  protein levels (4-fold), which. . . .

#### Candidate PPAR $\gamma$ Modulators

The following molecules and their derivatives and homologs are candidate PPAR $\gamma$  modulators:

- (1) HMG-CoA reductase inhibitors, including, but not limited to, **simvastatin**, **atorvastatin**, **pravastatin**, and **fluvastatin**
  - (2) Cholesterol and its metabolites such as the various oxysterols,
  - (3) Insulin and insulin mimetics,
  - (4) Glucocorticoid hormones, including, but not limited to, . . . including conditions involving skin (e.g., urticaria and eczema) and lungs (asthma), immunologic disorders (e.g., graft versus-host disease), parasitic infections, bacterial infections, and **viral** infections.
- Because PPAR $\gamma$  is highly expressed in cells involved in host defense, a modulator of PPAR $\gamma$  expression can be used to enhance. . . .

L19 ANSWER 2 OF 5 PCTFULL COPYRIGHT 2003 Univentio  
 ACCESSION NUMBER: 1999004238 PCTFULL ED 20020515  
 TITLE (ENGLISH): REAGENTS AND METHODS FOR DIAGNOSIS AND PROGNOSIS OF PROLIFERATIVE DISORDERS  
 TITLE (FRENCH): REACTIFS, PROCES DE DIAGNOSTIC ET PRONOSTIC DE TROUBLES PROLIFERATIFS  
 INVENTOR(S): PAGANO, Michele;  
 DRAETTA, Giulio;  
 ROLFE, Mark;  
 LODA, Massimo  
 PATENT ASSIGNEE(S): MITOTIX, INC.;  
 DEACONESS HOSPITAL;  
 PAGANO, Michele;  
 DRAETTA, Giulio;  
 ROLFE, Mark;  
 LODA, Massimo  
 LANGUAGE OF PUBL.: English  
 DOCUMENT TYPE: Patent  
 PATENT INFORMATION:  
 NUMBER KIND DATE  
 -----  
 WO 9904238 A2 19990128  
 DESIGNATED STATES  
 W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE  
 ES FI GB GE GH GM HR HU ID IL IS JP KE KG KP KR KZ LC

APPLICATION INFO.:  
PRIORITY INFO.:

LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU  
SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW GH  
GM KE LS MW SD SZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT  
BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF  
BJ CF CG CI CM GA GN GW ML MR NE SN TD TG  
WO 1998-US14566 A 19980714  
US 1997-08/893,276 19970715